UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,492	07/15/2002	Moulay A. Alaoui-Jamali	SWA-002US	3246

7590 03/19/2004

Law Offices of Wayne A Keown
500 West Cummunings Park
Woburn, MA 01801

EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	8

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,492	ALAOUI-JAMALI ET AL.	
	Examiner	Art Unit	
	Michele C. Flood	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Drawings

The drawings are objected to because the figures are not properly labeled. For example, the figures are labeled "1/4", "2/4", "2/4" and "4/4". However, the specification refers to the figures, as Figure 1, Figure 2, Figure 3 and Figure 4, respectively. It is suggested that Applicant replace "1/4", "2/4", "2/4" and "4/4" with Figure 1, Figure 2, Figure 3 and Figure 4, so that the labeling of the drawings correspond to the disclosure of the specification. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an anti-tumorogenic and anti-metastatic composition to treat malignant tumor and/or metastases comprising an extract isolated from *Achillea millefolium* and a suitable carrier, and an *in vivo* method for treating a malignant tumor and/or metastases thereof in mice bearing cancerous cells comprising administering an effective amount of an extract isolated from *Achillea millefolium* and a pharmaceutically acceptable carrier to mice in need thereof, does not reasonably provide enablement for an anti-tumorogenic and anti-metastatic composition to prevent malignant tumor and/or metastases comprising an extract isolated from *Achillea*

millefolium and a suitable carrier, and a method for preventing a malignant tumor and/or metastases in any and all patients comprising administering an effective amount of any and all extracts isolated from *Achillea millefolium* and a pharmaceutically acceptable carrier to any and all patients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, as broadly claimed.

The claims are directed to an anti-tumorogenic and anti-metastatic composition to treat and/or prevent malignant tumor and/or metastases thereof, said composition comprising a therapeutically effective amount of a substantially pure extract isolated from *Achillea millefolium* having antineoplastic activity, and a suitable carrier. The claims are directed to a method for treating and/or preventing a malignant tumor and/or metastases thereof in a patient, said method comprising administering to said patient a therapeutically effective amount of a substantially pure biologically active extract isolated from *Achillea millefolium* with a pharmaceutically acceptable carrier.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2D 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The specification is non-enabling for the claim designated method as the specification does not provide guidance as to how to identify and how to determine the solvents used in the making of the claimed designated plant extract, how to determine the plant parts used in the making of the claimed designated plant extract, and how to determine the effective therapeutic amounts of the claimed designated plant extract such that the plant extract is effective to prevent malignant tumor and/or metastases thereof. While it is possible that the composition, as recited in the claims, is useful for a method of treating, it seems highly unlikely that the claimed composition could be administered to any and all patients for preventing the claim-designated disease conditions comprising administering any and all extracts of *Achillea millefolium,* using any and all solvents and using any and all plant parts in the making of the claim-designated plant extract, even after extensive experimentation.

While the specification does demonstrate anti-tumor activity and anti-metastatic activity of varying concentrations for four fractions obtained from a methanolic extract of *Achillea millefolium* against Lewis Lung carcinoma cells and a method of treating a malignant tumor and/or inhibiting metastases thereof comprising administering therapeutically effective amounts of a methanolic extract of *Achillea millefolium* extract to mice bearing Lewis lung carcinoma cells, the specification does not disclose either a composition to prevent malignant tumor and/or metastases thereof or a method for preventing the claim-designated conditions comprising administering a therapeutically effective amount of the claim-designated plant extract. For example, in Figure 3 and in Figure 4, Applicant illustrates a dose-response relationship for the administration of a

methanolic extract obtained from *Achillea millefolium* and the inhibition of metastases in mice bearing Lewis lung carcinoma cells. However, no where in the disclosure of the specification does Applicant demonstrate a method for the prevention of the claim-designated disease conditions comprising the administration of the claim-designated plant extract.

At the time the invention was filed, the state of art recognized the anti-tumorogenic and anti-metastatic activity of extracts obtained from *Achillea millefolium* were known in the art of herbal medicine, as readily admitted by Applicant on page 2, lines 4-16 and as set forth in the rejections made under 35 U.S.C § 102 set forth below. However, the Office notes that malignant tumor diseases and metastases thereof are recognized in the art of medicine as diseases which are difficult to treat, much less prevent or eliminate. With regard to an extract of *Achillea millefolium* to prevent cancerous disease conditions even Applicant readily admits on page 2, lines 10-11 that at the time the invention was filed, the claimed functional effect was not known: "However, no proven anticancer activity [with regard to biologically active extracts of *Achillea millefolium*] has been reported." Yet, the specification broadly discloses an anti-tumorogenic and anti-metastatic composition to prevent malignant tumor and/or metastases thereof, wherein the composition comprises a therapeutic effective amount of a pure extract isolated from *Achillea millefolium* and a suitable carrier, and a method of use thereof for the prevention of the claim-designated disease conditions without support evidence. Although the claims do not expressly direct using an extract of *Achillea millefolium* for treating cancer or inhibiting the growth of cancer cells in

humans, the specification does teach delivering the claim-designated plant extract to mice bearing cancer cells, which are used in the art as an animal model to evaluate the therapeutic effectiveness of drugs used in the treatment of human disease conditions. On page 4, line 6 to page 5, line 4, the specification suggests that the active biologically extract of the claim-designated plant may be useful as a therapeutic and/or prophylactic treatment for various neoplastic conditions in humans, *e.g.*, cancer and leukemias. It should also be noted that the state of the art at the time of filing suggests that the delivery of therapeutic drugs which exhibit anti-tumor activity in murine cancer models do not necessarily have the same beneficial functional effect in humans as disclosed by Fredic Golden (Gorman, Christine. Cancer, "How to tell the hype from the hope: A Special Report", Time, May 1998, pages 37-46.) and as disclosed by Trisha Gura ("Cancer Models: Systems for Identifying New Drugs are Often Faulty", Science, 1997, Vol. 278, pages 1041-1042). Gura further discloses various different cancer models other than murine cancer models that are not predictive of the anti-cancer activity of potential anticancer agents when delivered to humans. In another instance, Jain (Jain, Rakesh K., Science, 1996, Vol. 271, pages 1079-1080, "Delivery of molecular medicine to solid tumors".) discloses that while promising chemotherapeutic agents exhibit activity against cancer cells *in vitro* and *in vivo* tumor systems, these same agents heralded as breakthrough drugs do not have the same functional effect in humans when delivered to humans bearing tumors.

Inventions targeted for cancer therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to

therapeutic treatments. Moreover, effective treatments for inhibiting or treating such disease conditions are relatively rare, and may be unbelievable in the absence of supporting evidence. Claims drawn to methods intended for the administration of compounds to cancer cells and/or cancer patients, or in the instant case, claims drawn to p compositions comprising plant extracts for the prevention of cancer and methods to prevent a malignant tumor and metastases thereof, generally require supporting evidence which clearly define the ingredients or constituents contained therein because of the unpredictability in biological responses to therapeutic treatments. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effective amounts of the extract intended for a therapeutic treatment for preventing the development of a malignant tumor and metastases thereof. There is no guidance in the specification, other than the aforementioned examples directed to the delivery of an effective amount of a methanolic extract from *Achillea millefolium* to mice bearing Lewis lung carcinoma cells. Given the insufficient guidance in the specification as to how to carry out the instantly claimed invention for the proposed method of therapeutic treatment, the lack of working examples, and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

Accordingly, it would take undue experimentation with out a reasonable expectation of success to prepare an extract isolated from *Achillea millefolium* having anti-tumorogenic and anti-metastatic activity, and it would take undue experimentation

with out a reasonable expectation of success to determine which amounts of the claim-designated composition would have the claimed functional effect to prevent malignant tumor and/or metastases thereof comprising administering to a patient a therapeutically effective amount of an extract isolated from *Achillea millefolium* and a pharmaceutically acceptable carrier to any and all patients, as broadly claimed by Applicant.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2-5 are rendered vague and indefinite by the term "extract" because this term, in and of itself, does not adequately delineate its metes and bounds. This term is best defined as a product-by-process since product-by-process claims are intended to define products which are otherwise difficult to define (and/or distinguish from the prior art). For example, is the extract obtained via extraction with water, a polar solvent, a non-polar solvent, an acid or base, a squeezed extract, or something else? In addition, from what part(s) of the plant is the extract obtained? It is well accepted in the herbal art that extraction with one of various distinct solvents, as well as from particular parts of therapeutic plants, has a profound impact on the final product with respect to the presence, absence, amounts, and/or ratios of active ingredients therein and, thus, its ability to provide the desired functional effect(s) instantly claimed

and/or disclosed. Since the extract itself is clearly essential to the claimed invention, the step(s) by which the claimed extract is obtained are also clearly essential and, therefore, must be recited in the claim language itself (i.e., as a product-by-process). Please note that although the claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., *In re* Van Guens, 988 F.2d 1181, 26 PSPG2d 1057 (Ded. Cir. 1991)). Accordingly, without the recitation of all these critical limitations as set forth above, the claims do not adequately define the instant invention.

The term "substantially" in claims 1, 4 and 5 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 3 provides for the use of an extract according to claim 2, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 3 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii et al. (C2, JP 62018139) and Tozyo et al. (C3, Chemical Pharmaceutical Bulletin, 1994, 42: 1096-1100.).

Applicant claims a substantially pure biologically active extract isolated from *Achillea millefolium*, said extract having an anti-tumorogenic and anti-metastatic activity. Applicant further claims an extract according to claim 1, said extract consisting of a crude methanol extract. Applicant claims an anti-tumorogenic and anti-metastatic composition to treat and/or prevent malignant tumor and/or metastases thereof, said composition comprising a therapeutically effective amount of a substantially pure extract isolated from *Achillea millefolium* having antineoplastic activity, and a suitable carrier.

Ishii (JP '139) and Tozyo teach a methanolic extract obtained from *Achillea millefolium* having anti-tumor action.

Each of the references of Ishii and Tozyo anticipate the claimed subject matter.

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii (N, JP 62081379).

Applicant's claimed invention of Claims 1, and 4 are set forth above. Applicant further claims Applicant claims a method for treating and/or preventing a malignant tumor and/or preventing a metastases thereof in a patient, said method comprising administering to said patient a therapeutically effective amount of a substantially pure biologically active extract isolated from *Achillea millefolium* with a pharmaceutically acceptable carrier.

Ishii (N, JP '379) teaches an anti-tumor agent isolated from *Achillea millefolium.* For example, a crude extract was extracted with methanol from the flowers of *Achillea millefolium* and subsequently purified twice by silica gel chromatography. Ishii further teaches a method for treating leukemia in mice transplanted with P388 leukemia comprising administering therapeutic amounts of the anti-tumor agent to mice, wherein the method increased by 38% and 48%.

The reference anticipates the claimed subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele C. Flood whose telephone number is (571) 272-0964. The examiner can normally be reached on 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele C. Flood

MICHELE FLOOD
PATENT EXAMINER

MCF
March 17, 2004